USE OF ELECTROMAGNETIC COUNTERPOISE TO MEASURE CARDIAC FORCE*

D.R. KULKARNI, P.V. DIWAN, L.D. TILLOO, P.A. PATIL AND M.K. BAGI

Department of Pharmacology,
J.N. Medical College, Belgaum-590010, Karnatak

Summary: To quantify the drug induced changes in cardiac force the methods in vogue use springs and strain-guage coils, which apply counterforce to oppose cardiac force and thus stop systolic excursion of the lever.

The present report pertains to a new technique based on similar principle, utilising induced electromagnetic force as a means of counterpoising in study of contractility of isolated frog heart. The technique monitered changes in contractility produced by small doses of adrenaline, digoxin, acetylcholine and $CaCl_2$. The plots of estimated cardiac force (in V) against doses (log-units) of the drugs could be made to reveal dose response relation.

The technique uses components simple to fabricate and work with; it is reliable and sensitive.

Key words: card iac force estimation, counterpoise afterloading, isometric tension, electromagnetic force

INTRODUCTION

Myocardial contractility is usually expressed in terms of some index associated with conditions of the experiment rather than in any fundamental units which relate to the muscle itself (4). From amongst the commonly used indices, isometric tension more faithfully depicts the state of contractility (2). Strainguage coils, arches and tension transducers are sophisticated gadgets employed to mesure isometric tension. These devices are expensive and often not easily available. Indeed, such a situation prompted us to fabricate and test the device described below, in which induced electromagnetic force is utilised for counterpoising cardiac force.

MATERIALS AND METHODS

Hearts isolated from frogs (Rana tigrina; 50-70 g weight) were perfused with Frog-Ringer at constant rate and pressure. All experiments were carried out at room temperature.

Myographic lever with an afterload screw was used to record isotonic heart beats. The lever was provided with a light-weight iron-shoe to over-hang the electromagnetic unit kept underneath.

A counterpoise unit was fabricated utilising an electromagnetic time-marker, a low voltage unit and a 'dimmerstat'. Inclusion of a voltmeter permitted assessment of voltage at any given time. Fig 1. shows the entire set up.

*Preliminary results were presented at III Southern Regional Conference, I.P.S., November, 1976 and the technique demonstrated in 'Pre-workshop in Research Methodology., 9th Annual Conference, I.P.S., Varanasi, December 1976

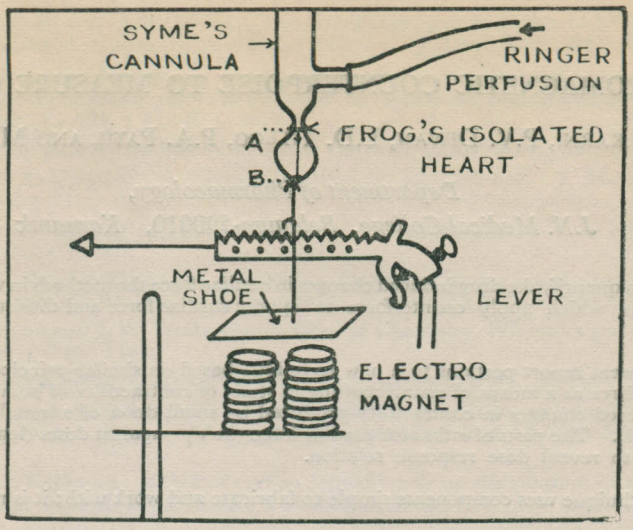

Fig. 1: Set-up of apparatus.
Note : Tension and shortening of A — B are recorded.

Setting-up of the preparation:

After the stabilisation of the heart over 20-30 min the after-load screw was positioned to permit fullest diastolic stretching for the given pressure and rate of perfusion. Then, the distance between the iron-shoe and the magnetic unit was adjusted to be narrow enough but never permitting actual contact between the two. The positions of the after-load screw and the magnetic unit so set were not disturbed till the end of the experiments.

Estimation of cardiac force:

After recording the isotonic contractions for a few min the electromagnet was activated and the intensity of generated magnetic force was swiftly increased by manipulating the current strength flowing through the magnet until the developed magnetic force was just enough to counter-balance the cardiac force and thus stop lever excursions. The voltage value was noted and magnet switched off. The procedure was repeated 3-4 times at five min intervals. The mean of the (voltage) readings provided an estimate of base-line (control period) cardiac froce.

Testing of drugs:

Procedure I : After noting the base-line cardiac force, the contractile force was again estimated when adrenaline (1-20 *ng*), $CaCl_2$ (50-800 μg) or acetylcholine (5-80 *ng*) produced peak effects as assessed from isotonic records. A mean of three separate measurements was calculated.

Procedure II : After noting the control cardiac force, the electromagnetic counterpoise was allowed to act continuously and cardiotonics like adrenaline (5-20 *ng*) or digoxin (10-50 *ng*) were given and the degree of recovery of lever excursions was noted.

In either of the procedures the interval between switch-on and switch-off of the magnet was 30-60 sec. The passage of current over such a short period did not cause any change in either the temperature or the resistance of the coil.

The volume of drug-solutions administered did not exceed 0.25 *ml*; in the case of digoxin however, the volume was 2-4 *ml*. Before administering the drug a saline control was obtained by giving frog-saline in volumes corresponding to drug volume.

Since the heart was perfused at constant rate and pressure and since the after-load screw was driven home before starting the estimation procedures it is very unlikely that tension-length relationship would influence and vitiate the estimated values.

Though the entire heart is mounted the force estimated corresponds to the isometric tension developed by the segment of the cardiac tissue between two fixed points (A-B of Fig. 1).

RESULTS

Procedure I : A total of 42 experiments were carried out. Adrenaline (Fig. 2), $CaCl_2$ and acetylcholine (Fig. 3) produced typical effects which were clearly measurable. Plots of estimated cardiac force against log-doses showed linear relationship; the dose-response curves were found to lie wide apart depending upon the drug, its dose and sensitivity of the heart (Fig. 4).

Procedure II : Digoxin produced a recovery (Fig. 5) of lever excursions (i.e. an increase in cardiac force). The procedure enabled the digoxin-inotropism to be demonstrated without a hypodynamic condition of the heart. In all the 10 experiments (Producere II) it was possible to observe cardiotonic effects of the drug in doses less than 50 *ng*. However, only in few experiments it was possible to establish dose-response relationship.

DISCUSSION

The inotropic effects of any drug is best described in terms of its influence on isometric tension development and force-velocity relations (3). The present technique monitors the former. The principle adopted has been that an after-load which just stops isotonic shortening represents isometric tension developed at that moment. It is well established that the imposed after-load that is exactly equal to the maximum tension (isometric) that the muscle is capable of developing prevents segment shortening (3,4).

In the present technique electromagnetic force has been used as an imposed after-load, the value of which reflects the isometric tention developed at the time of counterpoise. Since

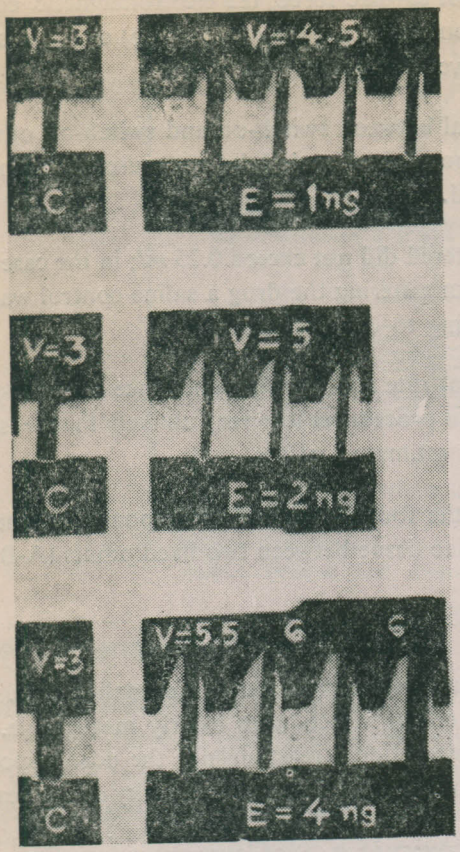

Fig. 2: Cardiogram showing effects of adranaline by Procedure I (See, text).
Upstroke-systole, C-control, E-Adrenaline, V-Voltage.
Note :
(i) Gaps in isotonic tracings indicate application of magnetic counterpoise to stop isotonic shortening.
(ii) Voltage values reflect magnetic force equalling cardiac force; these values increased with adrenaline dose.

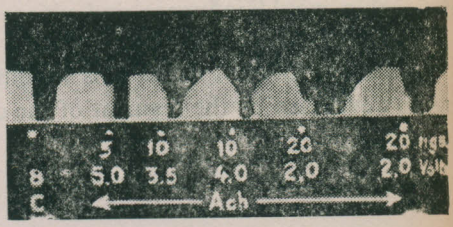

Fig. 3 : Cardiogram showing effect of acetylcholine by Procedure I (see. text).
C—control, Ach—acetylcholine.
Note: Voltage reflecting magnetic force decreases with increase in Ach dose.

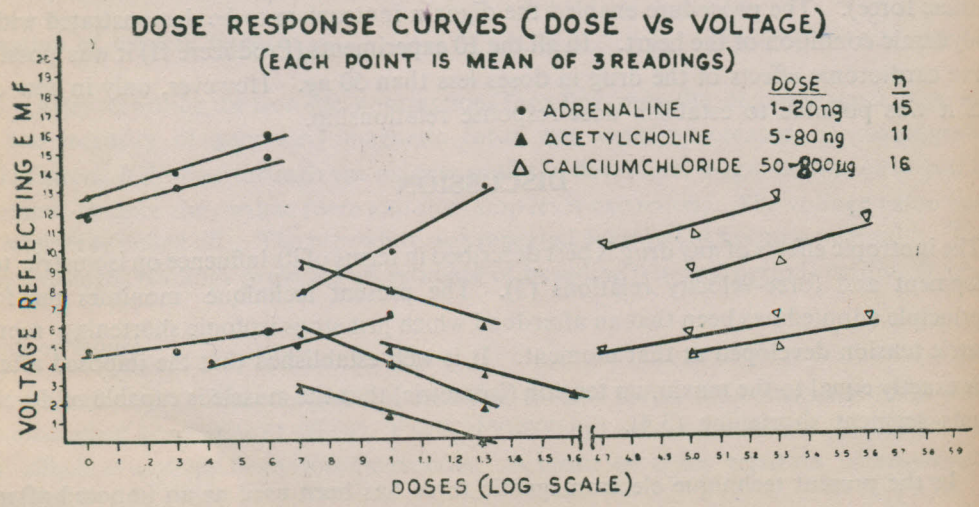

Fig. 4 : Few prototype dose response curves for acetylcholine, adrenaline and $CaCl_2$.
EMF = Generated electromagnetic force. n = number of experiments.

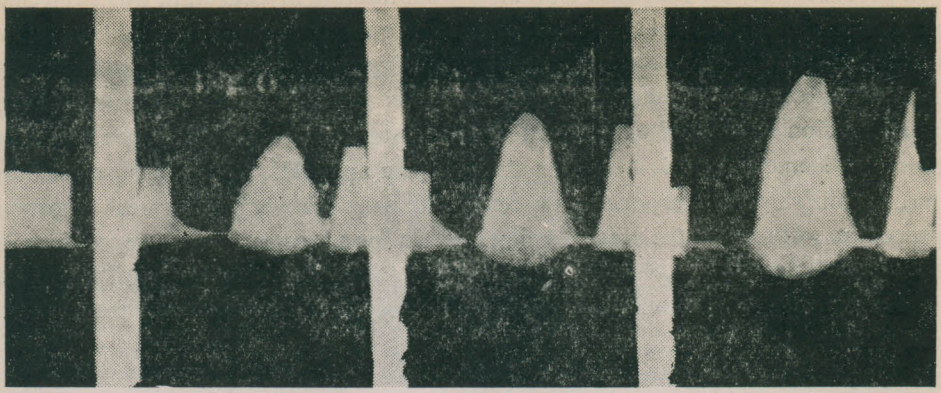

Fig. 5 : Cardiogram showing effects of digoxin by Procedure II (see, text).
Panels left to Right : Control, 1 ng., 2 ng., and 4 ng., digoxin.
Time interval between doses — 15 min.

the electromagnetic force has been used as imposed (counterpoising) after-load, Po (i.e. the after-load just sufficient to prevent shortening) should be expressed in terms of magnetic flux (force) given as :

$$\text{E.M.F.} = \frac{2\pi nC}{1Cr.}$$ where, E.M.F. = Electromagnetic force.

n = number of turns in the coil.

C = Current strength.

r = radius of the coil.

As long as the electromagnetic unit remains the same, changes in E.M.F. will be proportional to changes in C. Further, magnetic unit and its coil temperature remaining the same the resistance (R) of the coil also remains the same and therefore, the current strength (C) will be proportional to voltage (V), because, C = V/R. So, one can assume that when the same electromagnetic unit is used, Po can be expressed either in terms of E.M.F., current strength or voltage. In our experiments we have taken voltage values as estimate of E.M.F. and hence that of isometric tension.

In procedure I, an estimate of isometric tension was made during the control period as well as at the peak effect of drugs given in different doses. The changes in voltage values reflected changes produced by drugs in the development of isometric tension. There was linear relationship between log-doses and voltage values (Fig. 4) for positive inotropic drugs like adrenaline and $CaCl_2$ and the negative inotropic drug, acetylcholine. Further, the doses were in nanograms. We concluded therefore, that the method is reliable and sensitive.

In procedure II, the unloaded isotonically contracting myocardium was subjected to EMF counterpoise to abolish control systolic force. This counterpoise was allowed to act continuously for 30-60 sec during which period positive inotropic drugs, adrenaline or digoxin was given and percent recovery of segment shortening noted. This procedure does not involve counterpoise to measure tension developed subsequent to drug administration; and hence, can not provide an estimate of isometric tension developed after drug application. It is possible, however, to have this, if nullifying counterpoise is applied at the peak recovery of segment shortening. But such procedure will require the magnet being kept on for a longer time (i.e. more than 30-60 sec). With the magnetic coil we have used, such procedure lead to increase in coil temperature and hence in coil resistance. Therefore, in the present study (procedure II) only the percent recovery has been noted.

Excursion amplitude of isotonic contractions of actively beating normal heart does not increase much under the influence of digitalis (5). But digitalis-action on failing heart is much more impressive than on normal one (1). Hence, to demonstrate digitalis effect one employs heart rendered hypodynamic by perfusing Ringer containing less amount of $CaCl_2$ or Ringer having added barbiturates (1). In the present experiments with partial counterpoise (procedure II) actively beating normal heart also responded by increased force of contraction to digitalis administration.

The device is not meant as a substitute for more precise and acurate gadgets but is inexpensive, easily fabricable and fairly dependable for routine work.

ACKNOWLEDGEMENTS

The authors are grateful to Dean, Dr. B.S. Jirge and Principal, Dr. S.G. Desai for encouragement. We are also thankful to Mr. J.G. Dixit, Mr. M.D. Kankanawadi, Mr. S.S. Wandre, and Mr. A.V. Karvekar for their help and assistance in carrying out the work. We thank Prof. S.M. Hipparagi and Prof. G.V. Kulkarni, Department of Physics for their help. We also thank Mr. A.G. Naik, Mechanic, Department of Physiology, for help in assembling the magnetic unit.

REFERENCES

1. Crossland, J. Drugs that Act on Heart. In, *'Lewis's Pharmacology*, Ed. Crossland J. Edn IV, London, E & S Livingtone, P:891 and 902, 1970.
2. Katzung, B. Evaluation of Drugs Affecting the Contractility and Electrical Properties of the Heart, In: *'Selecled Pharmacological Testing Methods'*. Ed. Burger, A. Vol.3, New York, Marcel Dekkar Inc. P-196, 1968.
3. Parmley, W.W. and E. H. Sonnenblick. Cardiac Muscle Function Studies; In : *'Methods in Pharmacology'*, Ed. Schwartz A. Vol.1, New York, Appleton Century Crofts; p-107 and 112, 1971.
4. Thorp, R. H. and L. B. Cobbin. Methods for the Assessment of Cardiac Stimulant Substances (p.18) and "General Pharmacology of the Cardiac Glycosides" (p.75) : In *'Cardiac Slimulant Substances"* Ed. Thorp & Cobbin, New York, Academic Press, 1967.
5. Walton, R.P. Cardiac Glycosides, In : *'Pharmacology in Medicine'*, Ed. Drill. V.A., Edn.II, New York, McGraw-Hill Book Company. Inc., p:459, 1958.